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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 02/064759 A3

(54) Title: METHOD OF PROVIDING POLYPEPTIDE PREPARATIONS WITH REDUCED ENZYMATIC SIDE ACTIVITIES

(57) Abstract: A method of providing polypeptide preparations having a reduced content of undesired enzymatic side activities, the method comprising subjecting a medium containing a desired polypeptide such as an enzyme, a pharmaceutically active or immunologically active polypeptide to a pH of less than 2 for a period of time that is required to inactivate the side activities whilst retaining the activity of the desired polypeptide. The method is useful for providing milk clotting enzyme products including rennets or coagulants based on chymosin or pepsin or microbial aspartic proteases e.g. derived from bacterial species and species of filamentous fungi.

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/DK 02/00083

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 C12N9/99

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 C12N C12P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, EPO-Internal, PAJ, BIOSIS

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 20921 A (NOVONORDISK AS) 12 June 1997 (1997-06-12) page 8, line 7 - line 8; claims 1-8,13 page 15; example 6 ---	1-34
X	US 2 683 682 A (BYRON S.MILLER ET AL) 13 July 1954 (1954-07-13) column 1, line 26 - line 37 column 1, line 41 - line 44 column 1, line 55 -column 2, line 1 ---	1-34
A	US 3 950 221 A (KOKUSHO YOSHITAKA ET AL) 13 April 1976 (1976-04-13) column 2, line 36 - line 50 abstract ----	1-34

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

\* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

16 August 2002

Date of mailing of the international search report

23.09.2002

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**INTERNATIONAL SEARCH REPORT**International Application No  
PCT/DK 02/00083

<b>C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
<b>Category</b>	<b>Citation of document, with indication, where appropriate, of the relevant passages</b>	<b>Relevant to claim No.</b>
A	US 6 103 508 A (KATO ET AL) 15 August 2000 (2000-08-15) column 2, line 16 - line 19 abstract -----	1-34

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/DK 02/00083

### Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.: 33-34 because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
  
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

#### Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 33-34

Claims 33-34 relate to an extremely large number of possible compositions. The wording "essentially not having undesired enzymatic side activities" is vague and too broadly formulated to perform a complete search. Support in accordance with Article 6 PCT and disclosure in accordance with Article 5 PCT can, however, only be found for a very limited number of compositions. In the present case, the claims lack support, and the application lacks disclosure to such an extent, that a meaningful search over the whole of the claimed scope would be impossible. Consequently, the search has been limited to compositions provided by the method according to any of the claims 1-32. Claims 33-34 relate to a "product-by-process". However, there may be previously known compositions that have not been obtained by the method of claims 1-32 but that are identical to compositions according to claims 33-34.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

PCT/DK 02/00083

Patent document cited in search report		Publication date		Patent family member(s)		Publication date
WO 9720921	A	12-06-1997	AU CN WO EP US	1092297 A 1203627 A 9720921 A1 0865485 A1 6080564 A		27-06-1997 30-12-1998 12-06-1997 23-09-1998 27-06-2000
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